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10/597,155	07/13/2006	Yan Wang	17228.1	6856

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EXAMINER	
HISSONG, BRUCE D	
ART UNIT	PAPER NUMBER
1646	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/597,155	WANG ET AL.	
	Examiner	Art Unit	
	Bruce D. Hissong, Ph.D.	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 July 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1 and 3-12* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1 and 3-12* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Formal Matters

1. Application was received on 7/13/2006 and has been entered into the record.

2. Claims 1 and 3-12 are currently pending and are the subject of this office action.

Claim Objections

1. The Examiner suggests amending claim 7 to recite "polysorbate" rather than "polysrobate", "mannitol" rather than "mannit", and "ethyl acetate" rather than "ethyllacetate".

2. The Examiner suggests amending claim 10 to recite "dextran" rather than "dexcran".

3. The Examiner suggests amending claim 5 so as to clarify that the components listed on the left have the weights/amounts on the right. For example,

(i) phosphatide at 65-90 parts by weight

(ii) cholesterol at 50-30 parts by weight

(iii) stearic acid at 0.5-5 parts by weight

(iv) vitamin E at 0.2-2 parts by weight

A similar amendment is suggested for claim 7.

6. The Examiner suggests amending claim 6 to clarify that the ratio of the cited components is 80:18:1:1. For example, "The cream containing interferon encapsulated with liposome according to claim 5, wherein said liposome comprises phosphatide, cholesterol, stearic amide, and vitamin 5 at a weight ratio of 80:18:1:1.

A similar amendment is suggested for claim 10.

7. The Examiner suggests amending claim 11 to recite "natural or recombinant IFN-α, β, or γ" because natural IFN can encompass more than one type of IFN.

Claim Rejections - 35 USC § 112, second paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

1. Claim 1 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The claim recites a cream containing interferon, and further recites the limitation "in the case of greater than 80% efficiency of encapsulation." The intended meaning of this phrase is not clear; furthermore, it is also not clear what would be encompassed in cases where the efficiency of encapsulation is less than 80%.

2. Claims 7 and 10 contains the trademark/trade name Vaseline. Where a trademark or trade name is used in a claim as a limitation to identify or describe a particular material or product, the claim does not comply with the requirements of 35 U.S.C. 112, second paragraph. See *Ex parte Simpson*, 218 USPQ 1020 (Bd. App. 1982). The claim scope is uncertain since the trademark or trade name cannot be used properly to identify any particular material or product. A trademark or trade name is used to identify a source of goods, and not the goods themselves. Thus, a trademark or trade name does not identify or describe the goods associated with the trademark or trade name. In the present case, the trademark/trade name is used to identify/describe a component of a cream composition and, accordingly, the identification/description is indefinite.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

1. Claims 1, 3-4, and 11-12 are rejected under 35 U.S.C. 103(a) as being unpatentable over Foldvari (US 5,853,755).

The claims of the instant invention are drawn to a cream containing interferon (IFN) encapsulated with liposome, wherein the IFN is present in various cited amounts and having various cited ratios of biological activity to weight of cream substrate. The claims further recite a cream containing IFN encapuslated with liposomes, wherein said liposomes are made from various components and in specified percentages, and wherein said cream further comprises an excipient, an emulsifier, a stablizer, and an antiseptic.

Foldvari teaches compositions comprising IFNs in liposomes, wherein said compositions can be in the form of a cream (column 11, lines 20-25). Specifically, Foldvari discloses various agents that can be entrapped within liposomes, including IFN-α and IFN-γ (column 11, lines 16-17), and also teaches liposomes comprising lecithins, phopholipids, phosphatidylcholine (column 8, line 60 – column 9, line 17), cholesterol (column 9, lines 18-22), and further comprising agents such as glycerol and a "gel" (column 9, lines 31-41), polyoxyethylene (20) sorbitan monosterate or monooleate (also known as polysorbates 60 and 80, respectively, see http://en.wikipedia.org/wiki/Polysorbate_60) (column 12, line 59- column 13, line 19), and an antioxidant (column 8, lines 31-33).

Therefore, Foldvari teaches a cream composition comprising liposome encapsulated IFN-α or IFN-γ, wherein said liposomes may comprise lecithins, phospholipds, phosphatidylcholine, and/or cholesterol, and further comprise an antioxidant, but does not teach the specific ratios of IFN activity to weight of cream cited in the claims. However, one of ordinary skill in the art, at the time the instant invention was conceived, would have found it obvious, without undue experimentation, to optimize the amount of IFN in the cream in order to create the most effective therapeutic/pharmaceutical formulation. MPEP 2144.05 states:

"[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." *In re Aller*, 220 F.2d 454, 454, 105 USPQ 223, 235, (CCPA 1955).

In the instant case, the general conditions of a cream containing IFN-g or IFN-a in liposomes comprising lecithins, phospholipids, phosphatidylcholine, and/or cholesterol are disclosed in Foldvari.

2. Claims 5-6 are rejected under 35 U.S.C. 103(a) as being unpatentable over Foldvari (US 5,853,755), in view of Takahasi (US 2004/0258719), and further in view of Modi (US 6,193,997).

Claims 5-6 are drawn to the cream composition comprising IFN of claim 4, and further comprising phosphatide, cholesterol, stearic amide, and vitamin E at specific ratios.

The disclosure of Foldvari is discussed above. Foldvari does not specifically recite cream compositions comprising white and yellow vaselines, stearyl alcohol, stearic acid, paraffin, vitamin E, and antiseptics such as p-hydroxybenzoate. However, Takahashi teaches compositions for topical administration, and teaches creams comprising an active ingredient, and further comprising agents including white and yellow vaseline, stearyl alcohol, strearic acid, paraffin, tocopherols (i.e. vitamin E - see http://en.wikipedia.org/wiki/Tocopherol), and antiseptics such as p-hydroxybenzoate (see paragraph 0027). Takahashi does not each cream compositions comprising stearic amide.

However, Modi teaches liposome formulations which may comprise interferons as the active ingredient (column 5, line 12), and which also comprise a phospholipid such as lechitin (column 3, lines 60-66) and strearamide (column 3, line 46; stearamide = "stearic amide", see http://www.chemindustry.com/chemicals/1054350.html). Also taught is inclusion of tocopherol (i.e. vitamin E, column 4, line 65).

The motivation to create a cream composition comprising IFN encapsulated in liposome that meets the limitations of claim 4 is discussed above. One of ordinary skill in the art would also have further motivation to create a cream composition comprising liposome encapsulated IFN comprising phosphatides, cholesterol, strearic amide, and vitamin E/tocopherol because the combined teachings of Foldvari, Modi, and Takahashi show that these reagents are useful for liposome-based formulations. Specifically, Foldvari teaches liposomes comprising phosphatides and cholesterol, Modi teaches liposomes comprising strearamide/strearic amide and both Takahashi and Modi teach incorporation of tocopherols as antioxidants. Although neither Foldvari, Takahashi, nor Modi teach the specifically claimed ratios or amounts of each component, one of ordinary skill in the art, without undue experimentation, would be motivated and able to optimize the amounts of each component in order to create the most effective therapeutic/pharmaceutical formulation. MPEP 2144.05 states:

"[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." *In re Aller*, 220 F.2d 454, 454, 105 USPQ 223, 235, (CCPA 1955).

In the instant case, the general conditions of the claims are disclosed in Foldvari, Takahashi, and Modi, which collectively show that cream compositions comprising liposome encapsulated agents, such as IFN, can be formulated using phosphatides, cholesterol, stearic amide, and vitamin E.

3. Claims 7-9 are rejected under 35 U.S.C. 103(a) as being unpatentable over Foldvari (US 5,853,755), in view of Takahashi (US 2004/0258719), and further in view of Modi (US 6,193,997), and further in view of Shirley (US 2002/017261).

Claims 7-10 are drawn to the cream composition of claim 1, further comprising an excipient, an emulsifier, a stabilizer, and an antiseptic, wherein specific excipients, emulsifiers, stabilizers, and antiseptics are recited, as well as specific ratios or percentages of these agents.

The disclosures of Foldvari, Takahashi, and Modi are discussed above, but none of these references disclose IFN compositions comprising trehalose, sucrose, or mannitol. However, Shirley teaches IFN compositions comprising trehalose, mannitol, and/or sucrose as stabilizing agents (paragraph 0038).

The motivation to create a cream composition comprising IFN encapsulated in liposomes meeting the limitations of claim 1 is discussed above. One of ordinary skill in the art, at the time the instant invention was conceived, would have also been motivated to incorporate various excipients, emulsifiers, stabilizers, and antiseptics to the cream composition of claim 1. Takahashi in particular teaches creams with the claimed excipients white and yellow vaseline, stearic acid, lanolin, and paraffin, and also teaches incorporation of polysorbates 60 or 80, as well as the antiseptic p-hydroxybenzoate. Furthermore, Shirley teaches IFN compositions can be stabilized by the addition of sugars such as trehalose, mannitol, and/or sucrose (paragraph 0038), and also discloses the use of dextran (paragraph 0070). Thus, the available art, at the time of invention, disclosed cream compositions comprising liposome encapsulated IFN and further comprising the recited excipients, emulsifiers, stabilizers, and antiseptics, and therefore it would be obvious to one of ordinary skill in the art to incorporate these into the cream composition of claim 1. Although the ratio of polysorbate 80 to cream recited in claim 9 is not specifically taught, a person of ordinary skill in the art, without undue experimentation, would be motivated to optimize the polysorbate 80 concentration/ratio in the claimed cream composition in order to create the most effective therapeutic/pharmaceutical formulation. MPEP 2144.05 states:

"[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." *In re Aller*, 220 F.2d 454, 454, 105 USPQ 223, 235, (CCPA 1955).

In the instant case, the art discloses the general terms of a cream comprising liposome encapsulated IFN, and further comprising several of the recited excipients, emulsifiers, stabilizers, and antiseptics.

4. Claim 10 is rejected under 35 U.S.C. 103(a) as being unpatentable over Foldvari (US 5,853,755), in view of Takahashi (US 2004/0258719), in view of Modi (US 6,193,997), and further in view of Shirley (US 2002/017261), and further in view of Thompson *et al* (US 7,365,053).

Claim 10 is drawn to the formulation of claim 9, wherein the cream substrate comprises white vaseline, polysorbate 80, dexcran 40 (*sic* - interpreted to mean "dextran 40"), ethyl lactate, and p-hydroxybenzoate.

The teachings of Foldvari, Takahashi, Modi, and Shirley as they related to the obviousness of claim 9 are discussed above. These references do not disclose the use of ethyl acetate; however, Thompson shows that ethyl acetate is a useful stabilizer/solvent for use with microparticle emulsions/liposomes (abstract; column 27, line 28; column 28, line 59). Therefore, a person of ordinary skill in the art, at the time the present invention was conceived, would have been motivated to create a cream composition comprising liposome encapsulated IFN and further comprising white vaseline, polysorbate 80, dextran 40, ethyl acetate, and p-hydroxybenzoate because the prior art teaches that these substances are useful for use with liposome compositions. Although the art does not explicitly teach the recited ratio of vaseline, polysorbate 80, dextran 40, ethyl acetate, and p-benzoate, one of ordinary skill in the art, without undue experimentation, would be motivated to optimize the concentration/ratios of these agents in order to create the most effective therapeutic/pharmaceutical formulation. MPEP 2144.05 states:

"[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." *In re Aller*, 220 F.2d 454, 454, 105 USPQ 223, 235, (CCPA 1955).

In the instant case, the art discloses the general terms of a cream comprising liposome encapsulated IFN, and further comprising white vaseline, polysorbate 80, dextran 40, ethyl acetate, and p-hydroxybenzoate.

Conclusion

No claim is allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bruce D. Hissong, Ph.D., whose telephone number is (571)272-3324. The examiner can normally be reached M-F from 8:30 am - 5:00 pm. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Nickol, Ph.D., can be reached at (571) 272-0835. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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